Legal Division - Patent Department
J. Michael Dixon
Pfizer Inc
2800 Plymouth Road
Ann Arbor, MI 48105
Tel 734 622 1705 Fax 734 622 1553



European Patent Office
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Authorized Officer: Zellner, A

April 14, 2005

Re: International Application No. PCT/IB2004/003668
Warner-Lambert Company LLC
Docket No. PC26158

RESPONSE TO WRITTEN OPINION OF
INTERNATIONAL SEARCHING AUTHORITY

Dear Sirs,



This communication is being submitted in response to the Written Opinion of the International Preliminary Examining Authority ("IPEA"). The IPEA has rejected claims 1, 4, 5 and 6 as lacking novelty in view of references D1-D4. Claim 9 is being treated as a method claim and is rejected as lacking utility. The IPEA has stated that the remaining claims are novel and possess an inventive step in light of references D1-D6.

In order to advance the prosecution of this application, claims 1 and 9 have been amended. The definition for $R^1$ has been amended to exclude halogen. $R^1$ must now be represented by a haloalkyl or haloalkoxy moiety. The claims only read on 2-amino-5-cyano-pyridines that are further substituted at positions 3 or 4 with a haloalkyl or haloalkoxy moiety. Position 6 of the pyridine core may still be optionally be substituted with a halogen. It is respectfully submitted this amendment removes any overlap with references D1-D4.

Claim 9 has now been converted into a Swiss-use claim. Substitute sheets 37 - 40 reflecting the amendments described above accompany this report. An International Preliminary Examination Report confirming the patentability of claims 1-14 is hereby requested.

Respectfully submitted,

4/14/05
Date

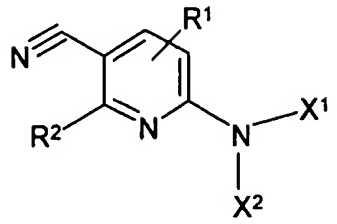
J. Michael Dixon
Attorney for Applicant(s)
Reg. No. 32,410

Warner-Lambert Company
Patent Department (421W)
2800 Plymouth Road
Ann Arbor, MI 48105
(734) 622-1705

CLAIMS

What is claimed is:

1. A compound of the formula:



and the pharmaceutically acceptable salts, hydrates, and prodrugs thereof, wherein;

a) $R^1$ is represented by $(C_1\text{-}C_2)$alkyl, substituted with one or more halogens, or $(C_1\text{-}C_2)$alkoxy, substituted with one or more halogens,

b) $R^2$ is represented by hydrogen or halogen,

c) $X^1$ and $X^2$ are each independently represented by

i) $(C_1\text{-}C_{12})$alkyl, optionally substituted,

ii) $(C_2\text{-}C_{12})$alkenyl, optionally substituted,

iii) $(C_2\text{-}C_{12})$alkynyl, optionally substituted,

iv) $(C_3\text{-}C_{10})$cycloalkyl, optionally substituted,

v) $(C_3\text{-}C_{10})$cycloalkyl$(C_1\text{-}C_6)$alkyl, in which the alkyl and cycloalkyl moieties may each be optionally substituted,

vi) $(C_6\text{-}C_{10})$aryl, optionally substituted,

vii) $(C_6\text{-}C_{10})$aryl$(C_1\text{-}C_6)$alkyl, in which both the alkyl and aryl moieties may be optionally substituted,

viii) $-(CH_2)_q\text{-}CH_2\text{-}ZH$, in which Z is S or O and q is an integer from 1-11,

ix) $-(CH_2)_n\text{-}Y\text{-}(CH_2)_p\text{-}CH_3$, in which Y is O or S, n is an integer from 1 to 4, and p is an integer from 1 to 4,

x) $-[CH_2]_m\text{-}C(O)R^3$, in which m is an integer selected from 1 to 8 and $R^3$ is represented by hydrogen, $(C_1\text{-}C_{12})$alkyl, $(C_6\text{-}C_{10})$aryl, or $(C_6\text{-}C_{10})$aryl$(C_1\text{-}C_6)$alkyl, in which both the alkyl and aryl moieties may be optionally substituted,

xi) $-[CH_2]_m\text{-}C(O)\text{-}O\text{-}R^4$, in which m is as defined above and $R^4$ is represented by hydrogen, $(C_1\text{-}C_{12})$alkyl, $(C_6\text{-}C_{10})$aryl, or

$(C_6$-$C_{10})$aryl$(C_1$-$C_6)$alkyl, in which the alkyl and aryl moieties may be optionally substituted,

xii) -$[CH_2]$m-C(O)-$NR^5R^6$ in which m is as described above, and $R^5$ and $R^6$ are each independently represented by hydrogen, $(C_1$-$C_{12})$alkyl, $(C_6$-$C_{10})$aryl, or $(C_6$-$C_{10})$aryl$(C_1$-$C_6)$alkyl, in which the alkyl and aryl moieties may each be optionally substituted,

i) heteroaryl, optionally substituted,

ii) heteroaryl$(C_1$-$C_6)$alkyl, in which the heteroaryl and alkyl moieties may each be optionally substituted,

iii) heterocyclic, optionally substituted, or,

iv) heterocyclic$(C_1$-$C_6)$alkyl, in which the alkyl and heterocyclic moieties may each be optionally substituted.

2. A compound according to claim 1 in which R is represented by trifluomethyl.

3. A compound according to any one of claim s 1- or 2 in which said trifluoromethyl is located at the 4-position of the pyridine ring.

4. A compound according to anyone of claims 1-3 in which $R^2$ is hydrogen.

5. A compound according to anyone of claims 1-4 in which $X^1$ is $(C_1$-C12)alkyl and X2 is (C6-C10)aryl(C1-C6)alkyl.

6. A compound according to anyone of claims 1-5 in which $X^1$ and $X^2$ are each $(C_1$-$C_{12})$alkyl

7. A compound according to anyone of claims 1-6 in which $X^1$ is $(C_1$-$C_{12})$alkyl and X 2 is (C3-C10)cycloalkyl(C1-C6)alkyl.

8 A compound according to claim 1 selected from the group consisting of ( R )-(+)- 6-[Methyl-(1-Phenyl-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,

( R)-(+)-2-Chloro-6-[methyl-(1-phenyl-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,

6-[methyl-(1-phenyl-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,
6-[methyl-(1-phenyl-ethyl)-amino]-4-trifluoromethoxy-nicotinonitrile,
6-[methyl-(1-(4-fluorophenyl)-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,
6-[methyl-(1-(3-hydroxyphenyl)-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,
6-[butyl(1-(3-hydroxyphenyl)-ethyl)-amino]-4-trifluoromethoxy-nicotinonitrile,
6-dipropylamino-4-trifluoromethyl-nicotinonitrile,
2-chloro-6-dimethylamino-4-trifluoromethyl-nicotinonitrile,
6-(hexyl-octyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-(sec-butyl-methyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-[butyl-(2-hydroxy-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile,
6-(butyl-methyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-(benzyl-methyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-(cyclohexyl-propyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-(cyclopropylmethyl-propyl-amino)-4-trifluoromethyl-nicotinonitrile,
6-(sec-butyl-methyl-amino)-2-chloro-4-trifluoromethyl-nicotinonitrile,
6-Dipropylamino-2-chloro-4-trifluoromethyl-nicotinonitrile,
6-(propyl-methyl-amino)-2-chloro-4-trifluoromethyl-nicotinonitrile, and,
6-(Butyl-methyl-amino)-2-chloro-4-trifluoromethyl-nicotinonitrile.



9. Use of a compound according to anyone of Claims 1-8 in the manufacture of medicament.

10. Use of a compound according to anyone of Claims 1-8 in the manufacture of a medicament for inhibiting activation of the androgen receptor.

11. A pharmaceutical composition comprising a compound according to any one of Claims 1-8 in admixture with 1, or more, pharmaceutically acceptable excipients.

12. A topical pharmaceutical formulation comprising a compound according to anyone of Claims 1-8 in admixture with 1, or more, pharmaceutically acceptable excipients suitable for dermal application.

13. An article of manufacture comprising a compound according to any one of Claims 1-8 packaged for retail distribution which advises a consumer how to utilize the compound to alleviate a condition selected from the group consisting of acne, alopecia, and oily skin.

14. Use of a compound according to any one of claims 1-8 in the manufacture of a medicament for alleviating a condition selected from the group consisting of hormone dependent cancers, benign hyperplasia of the prostate, acne, hirsutism, excess sebum, alopecia, premenstrual syndrome, lung cancer, precocious puberty, osteoporosis, hypogonadism, age-related decrease in muscle mass, and anemia.